REMARKS

Claims 1,6, 9-11 and 16 currently are pending in this application. Claim 1 has been amended. Claim 16 has been added. Support for the language in claim 16 is found in original claim 1 and at page 9, second paragraph, of the specification. No new matter has been added.

Summary of Examiner's Interview

The undersigned representative of the applicants, Dr. Wood, wishes to thank the Examiner for the courtesies extended during the telephonic interview conducted on May 21, 2009, in which Dr. Dean Mann also was in attendance.

In the interview, Dr. Mann first provided an historical background regarding the unexpected finding that administration to a mammal of culture medium supernatant, referred to as lymphocyte conditioned medium (LCM), derived from activated peripheral blood mononuclear cells (PBMCs) enhances the immune response to the antigen in the mammal. Dr. Mann stated that he and other investigators infused activated T-cells into patients receiving bone marrow transplants to see if these cells would enhance the patient's response to an antigen. They surprisingly found that the patient's immune response to an antigen was augmented, but it was not the cells themselves that were responsible for this augmentation to an antigen, but rather the products of the activated T cells, that is, cytokines and chemokines, released from the activated T cells that was responsible for enhancing the immune response to an antigen in these patients. They proceeded to administer to rhesus monkeys the culture products contained in the supernatant of activated T cells in combination with an antigen, and showed an enhanced immune response to the antigen.

Dr. Wood stated that none of the prior art references discloses administering to a mammal supernatant of activated cells in combination with an antigen to augment the immune response to the antigen in the mammal. Dr. Mann agreed with this, stating that, to his knowledge, he is not aware of any

publication by other investigators showing that the administration of culture products of activated T cells, in combination with an antigen, enhances the immune response to the antigen.

We discussed the Kato et al. reference, in which Dr. Wood pointed out that this reference solely discloses administering antigen-loaded dendritic cells to enhance immunity, and using supernatant from activated T cells to induce differentiation of immature dendritic cells. Dr. Mann stated that such disclosures are not new and have been known for at least ten years.

We discussed entering new claim 16 and amending claim 1 to recite the limitations of new claim 16. The Examiner asked for clarification regarding the difference between new claim 16 and claim 1 that was submitted on November 16, 2007, as she wanted to avoid sending out another rejection. Dr. Wood pointed out that claim 1 does not recite a supernatant derived from activated PBMCs, but rather LCM derived from naïve T-cells. Dr. Wood further stated that activation of PBMCs results in culture products that are responsible for the enhanced immune response. The Examiner acknowledged the difference between the claims, noting that claim 16 recites the source of the cells and that the cells are activated to produce culture products in the supernatant responsible for enhancing an immune response to an antigen. The Examiner stated that the current rejections would no longer apply and that she would conduct a new search based on the new and amended claim(s).

35 U.S.C. 112 Rejection

Claim 1 has been amended to delete recitation of the phrase "such as," and thus this rejection is moot.

35 U.S.C. 103(a) Rejections

Claim 1 is rejected as being obvious over of Kato et al. in view of Mengozzi et al.; claim 6 is rejected as being obvious over Kato et al. in view of Mengozzi et al. and Meidenbauer et al.; and claims 9-11 are rejected as obvious over Kato et al. in view of Mengozzi et al. and Setaluri et al.

Respectfully, applicants submit that Kato, Mengozzi, Meidenbauer and Setaluri, neither alone nor in combination, disclose or even remotely suggest the claimed invention, which provides a method of enhancing an immune response to an antigen in a mammal by administering to the mammal a vaccine comprised of an antigen and culture medium supernatant (i.e., LCM) derived from PBMCs activated with anti-CD3- and anti-CD28-coated beads in the culture medium.

Rather, Kato discloses using supernatant from activated T cells to induce differentiation of immature dendritic cells and administration of antigen-loaded dendritic cells to enhance immunity. Kato is completely silent with respect to administering culture medium supernatant (i.e., LCM) in combination with an antigen to a mammal to enhance immunity to the antigen.

Mengozzi discloses using anti-CD3/anti-CD28-coated beads *ex vivo* to stimulate T cells and to culture naïve T cells, and thus does not cure the deficiencies of Kato to teach the claimed invention as required by claim 1 and new claim 16.

In addition, attached herewith is an expert's Declaration by Dr. Dean Mann, who attests to the surprising and unexpected finding that culture medium supernatant derived from activated PBMCs, which contains culture products such as cytokines and chemokines, augments the immune response to an antigen *in vivo*. In clinical trials, Dr. Mann and colleagues infused anti-CD3/anti-CD28 activated T cells into patients to see if the activated T cells would enhance a patient's response to an antigen. They found that a patient's immune response to an antigen was augmented, but could not identify antigen-specific memory T cells in the infused cell population. They subsequently found that the culture products released from the activated T cells could account for the enhanced immune response to an antigen in the patient.

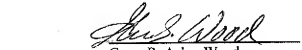
Dr. Mann further attests that, to the best of his knowledge, he is not aware of any research studies or publications by other investigators which show that culture products of PBMCs activated by anti-CD3/anti-CD28 enhance immune responses in mammals when administered as an adjuvant to an antigen.

In view of the fact that Kato and Mengozzi do not teach or even suggest a method of enhancing an immune response to an antigen in a mammal by administering to the mammal a vaccine comprised of an antigen and culture medium supernatant derived from PBMCs activated with anti-CD3- and anti-CD28-coated beads in the culture medium, as required by claims 1 and 16, it is respectfully submitted that claims 1 and 16, and claims 6 and 9-11, which depend directly from claim 1, are most clearly drawn to patentable subject matter, and such action is respectfully sought.

If the Examiner wishes to discuss any aspect of this response, the Examiner is invited to contact the undersigned at the telephone number indicated below.

Applicants believe that fees for a three-month extension of time are due with this filing. Such fee is being simultaneously paid via electronic funds transfer with this submission. The Commissioner is hereby authorized to charge any additional fees required or to credit any overpayment to Deposit Account 20-0809. The applicant(s) hereby authorizes the Commissioner under 37 C.F.R. §1.136(a)(3) to treat any paper that is filed in this application which requires an extension of time as incorporating a request for such an extension.

Respectfully submitted,



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